IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Osama Kandil	:	Confirmation No.: 7603
Serial No.: 10/809,869	:	Group Art Unit: 1609
Filed: March 26, 2004	:	Examiner: Samira JEAN-LOUIS

For: POLYUNSATURATED FATTY ACID FRACTIONS OF NIGELLA SATIVA L. SEEDS

Attorney Docket No.: KAN-001-B

Mail Stop **AF**
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

TRANSMITTAL LETTER

Dear Sir:

Please find the following correspondence items submitted for filing with the United States Patent and Trademark Office by EFS-WEB on the date shown below:

1. Notice of Appeal; and
2. Pre-Appeal Brief Request for Review.

Respectfully submitted,

Date: /April 1, 2009/

By: ____/chalin a. smith/___

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PRE-APPEAL BRIEF REQUEST FOR REVIEW

Sir:

Applicant hereby requests that a panel of examiners be convened to formally review the legal and factual basis of the rejections in the instant application in accordance with the procedures outlined in the OG Notice of July 12, 2005. Applicant respectfully submits that the Final Rejection of November 7, 2008 is fundamentally flawed, lacking both legal and scientific foundation. Further to this position, Applicant submits the enclosed remarks (no longer than 5 pages) and respectfully petitions for reconsideration of the outstanding grounds of rejection in view of the arguments therein. Applicant further petitions for the summary issuance of a notice of allowance in view of the following remarks:

REMARKS

Pursuant to the entry of the terminal disclaimer filed March 9, 2009, the only remaining rejections are the prior art rejections of elected claims 9-11, 15, 18-21, and 26-29, namely:

- The final rejection of claims 9-11, 15, 18-21, and 26 under 35 U.S.C. § 103(a) as being obvious over Ahmad et al. (US 2005/0058735) in view of Berg (Advances in Dermatology, 1988);
- The final rejection of claims 28-29 under 35 U.S.C. § 103(a) as being obvious over Ahmad et al. (US 2005/0058735) in view of Berg (Advances in Dermatology, 1988) and Nickavar (Naturforsch, 2003); and
- The final rejection of claim 27 under 35 U.S.C. § 103(a) for being obvious over Ahmad et al. (US 2005/0058735) in view of Berg (Advances in Dermatology, 1988), Schlenk et al. (JACS, 1950), and Ali et al. (PTR, 2002).

While Applicant takes issues with each of the above rejections, the primary point of contention surrounds the Examiner's interpretation of the teachings of the primary reference to Ahmad, in particular, her suggestion that Ahmad provides the requisite connection between *Nigella sativa* extracts and skin diseases. Applicant's position on the proper interpretation of Ahmad is set forth at length in the responses January 8, 2008 (p. 10-11) and August 1, 2008 (p. 8-12) and summarized hereinbelow:

1. **Ahmad does not suggest to one of ordinary skill in the art the use of *Nigella sativa* extracts for the treatment of skin diseases.**

The Ahmad reference mentions the word "skin" exactly twice – once in paragraph [0019], wherein he notes in passing that "many members of the family *Ranunculaceae* can be used for treatment of a variety of conditions, including *skin diseases*, hemorrhoids, cancer, endothelial cell progression, decrease in the production of the angiogenic protein-fibroblastic growth factor made by tumor cells and inhibition of the growth factor made for endothelial cells", and a second time in paragraph [0005], wherein "skin" reactions are mentioned as possible negative side effects of interferon therapy. The fact that "many members" of the family *Ranunculaceae* have certain known applications does not serve as a teaching that one specific botanical composition (i.e., a polyunsaturated fatty acid fraction extracted from *Nigella sativa*) is suitable for use in the treatment of one of the specifically mentioned disorders (i.e., skin

conditions such as diaper rash). In that the remainder of the Ahmad disclosure is directed to novel applications for combinations of extracts obtained from members of the Family:Ranunculaceae, Subclass: Dicotyledonae or Crassinucelli, Superorder: Ranunculales in the treatment of liver and immunological disorders, more particularly hepatitis, Applicant respectfully submits that Ahmad fails to disclose or suggest a method of treating or preventing *any* skin condition with a *Nigella sativa* extract.

2. The genus does not fairly suggest the claimed species.

At the time of the invention of Ahmad et al., people had been experimenting for decades with *Ranunculaceae* plants and to date had discovered a variety of therapeutic uses thereof, such uses ranging from the treatment of "fevers, boils, and rheumatism" (Ahmad, [0018]) to the treatment of conditions such as "skin diseases, hemorrhoids, cancer, endothelial cell progression, decrease in the production of the angiogenic protein-fibroblastic growth factor made by tumor cells and inhibition of the growth factor made for endothelial cells" (Ahmad, [0019]). However, the *Ranunculaceae* family consists of 51 to 88 genera, totaling about 2500 species. While Ahmad et al. highlight the use of *Nigella sativa*, preferably in combination with one or more extracts from the genera *Actaea*, *Anemone*, and *Ranunculus*, they do so solely in the context of immunomodulation and the treatment of liver diseases, particularly those with viral etiology (e.g.. hepatitis). Nowhere in the Ahmad reference is there a suggestion that, of all the species of *Ranunculeae*, of all the potential pharmaceutical uses thereof, it is desirable to utilize the extracts of *Nigella sativa* in the treatment of skin diseases. In fact, Applicant submits that the likelihood of arriving at a method comprised of these select variables "would be the same as discovering the combination of a safe by the inspection of its dials". *Ex parte Garvey*, 41 USPQ 583 (POBA 1939); *Ex parte Starr*, 44, USPQ 545 (POBA 1938).

Moreover, even if one does construe Ahmad as arguably suggesting that "members" of *Ranunculaceae* "can be used" for the treatment of "skin diseases", there is no clear teaching of selecting one specific extract component (i.e., a purified polyunsaturated fatty acid fraction extracted from *Nigella sativa* L. seeds), formulating it as a topically administrable, semi-solid composition and using it the treatment of skin disorders, much less a specific type of skin disorder (e.g., skin conditions arising from fungal infection, bacterial infection, allergic reaction or inflammation). Accordingly, Applicant submits that not only would one of skill in the art not

have been motivated by the generic teachings of Ahmad to select *Nigella sativa* for further consideration in the context of the topical treatment of skin disease but he would further not have been motivated to combine the Ahmad teachings with those of Berg to arrive at the invention of the pending claims.

3. There is no reasonable expectation of success.

Obviousness requires at least a reasonable degree of predictability. Herein, the Examiner suggests that it would merely be a matter of routine to utilize the Ahmad extract compositions in the treatment of *any* skin condition, including diaper rash, despite the fact that the entirety of the Ahmad reference relates to the treatment of liver and immunological disorders, particularly hepatitis C (HCV). Given the wide variability within the genus of "skin diseases", a genus encompassing hundreds of divergent conditions ranging from acne to warts, and the admitted lack of predictability in the art[1], Applicant submits that one could not reasonably have predicted the efficacy of a purified polyunsaturated fatty acid fraction extracted from *Nigella sativa* and formulated for topical administration with a suitable pharmaceutical carrier in the treatment of those select skin conditions arising from fungal infection, bacterial infection, allergic reaction or inflammation merely from the disclosure that some of the 2500 different species of *Ranunculaceae* botanical are known for the treatment of "skin diseases".

4. Ahmad does not fairly suggest "semi-solid" formulations.

While the Ahmad compositions are generically described as suitable for "oral, parenteral, topical, and nasal delivery as well as by suppository, contemplating solid dosage-forms, liquids, suspensions, intramuscular, subcutaneous, intravenous, and transdermal delivery systems", all the examples and preferred embodiments relate to the treatment of hepatitis C with an intramuscular injection preparation. Accordingly, given that neither skin diseases nor topical administration is separately identified by Ahmad et al. as preferred or illustrated in any of the recited examples, much less identified as useful together, Applicant respectfully submits that one could arrive at the presently claimed combination only through a meticulous selection of substituents for which Ahmad provides no motivation or guidance, something akin to finding a

[1] In the Restriction Requirement of July 10, 2007, the Examiner characterized the treatment of skin conditions as "unduly unpredictable", noting that various known skin conditions are characterized by "different etiologies" and "different mechanisms of action".

needle in a haystack. Given these limitations, Applicant respectfully submits that one of ordinary skill in the art would not have been motivated to combine the teachings of Ahmad et al. with those of Berg et al. to provide a semi-solid composition formulated for topical administration comprising a polyunsaturated fatty acid fraction extracted from *Nigella sativa* L. seeds and a pharmaceutically acceptable carrier.

5. Neither Ahmad nor Berg not fairly suggest "a purified polyunsaturated fatty acid fraction extracted from *Nigella sativa* L. seeds".

Ahmad discloses the use of crude extracts, i.e., ground plant material extracted in a polar solvent and subsequently vacuum concentrated (Ahmad, [0065]). As such, the Ahmad extract is comprised of numerous components, including fatty acids, glyceryl esters, volatile oils, and total sterols (see Applicant's Figure 1), components expressly excluded from pending claims 15 and 27. In contrast, the *Nigella sativa* extract of the presently claimed invention comprises a purified polyunsaturated fatty acid fraction, e.g., saponified using 10% ethanolic KOH and subjected to the urea inclusion process several times so as to yield a fraction substantially devoid of contaminants (again, referring to Applicant's Figure 1, steps 4-7). Accordingly, Applicant respectfully submits that neither Ahmad nor Berg discloses the use of a semi-solid composition formulated for topical administration comprising a purified polyunsaturated fatty acid fraction extracted from *Nigella sativa* L. seeds and a pharmaceutically acceptable carrier.

CONCLUSION

In sum, Applicant submits that the Final Rejection of November 7, 2008 contains fundamental and clear errors, untenable positions that cannot withstand the scrutiny of appeal.

Respectfully submitted,

Date: /April 1, 2009/

By: ____/chalin a. smith/___

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APPENDIX A: CLAIMS AT ISSUE

Claims 1 – 8 (Withdrawn)

9. (Previously Presented) A method of treating a skin condition arising from fungal infection, bacterial infection, allergic reaction, or inflammation in a patient in need thereof comprising topically administering an effective amount of a semi-solid composition formulated for topical administration comprising a purified polyunsaturated fatty acid fraction extracted from *Nigella sativa* L. seeds and a pharmaceutically acceptable carrier.

10. (Previously Presented) The method of claim 9, wherein the semi-solid composition has skin moisturizing, revitalizing, and analgesic effects.

11. (Previously Presented) The method of claim 9, wherein the skin condition is selected from the group consisting of psoriasis, eczema, dermatitis, dry, scaly, itchy or flaky skin, diaper rash, athlete's foot, jock itch, scalp irritations, and dermal infections.

Claims 12 – 14 (Withdrawn)

15. (Previously Presented) The method of claim 9, wherein the polyunsaturated fatty acid fraction consists essentially of polyunsaturated fatty acids.

Claims 16 – 17 (Withdrawn)

18. (Previously Presented) The method of claim 26, wherein the polyunsaturated fatty acid fraction is present in an amount ranging from about 15 to about 28% by weight based on 100 parts by weight of the total composition.

19. (Original) The method of claim 18, wherein the polyunsaturated fatty acid fraction is present in an amount ranging from about 18 to about 25% by weight based on 100 parts by weight of the total composition.

20. (Original) The method of claim 19, wherein the polyunsaturated fatty acid fraction is present in an amount ranging from about 20 to about 23% by weight based on 100 parts by weight of the total composition.

21. (Previously Presented) The method of claim 9, wherein the composition further comprises at least one compound selected from the group consisting of an emulsifying agent, a stabilizing agent and a preservative.

Claims 22 – 25 (Withdrawn)

26. (Previously Presented) The method of claim 9, wherein the semi-solid composition contains from about 1 to about 33% by weight polyunsaturated fatty acid fraction, based on 100% by weight of the total composition.

27. (Previously Presented) The method of claim 9, wherein the polyunsaturated fatty acid fraction is free of *Nigella sativa* L. saturated fatty acids, sterols, volatile oils, and glyceryl esters.

28. (Previously Presented) The method of claim 9, wherein the polyunsaturated fatty acid fraction consists essentially of octadecadienoic acid and octadecenoic acid.

29. (Previously Presented) The method of claim 28, wherein the octadecadienoic acid is present in the polyunsaturated fatty acid fraction in an amount ranging from about 60.7 to about 72.6% by weight, and the octadecenoic acid is present in the polyunsaturated fatty acid fraction in an amount ranging from about 23.8 to about 29.7% by weight.